THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

FY 2000 INVESTMENTS

Improving the Nation's Health
Through Medical Research on
Prevention, Diagnosis, and Treatment

September 7, 2000

National Heart, Lung, and Blood Institute

FY 2000 Investments

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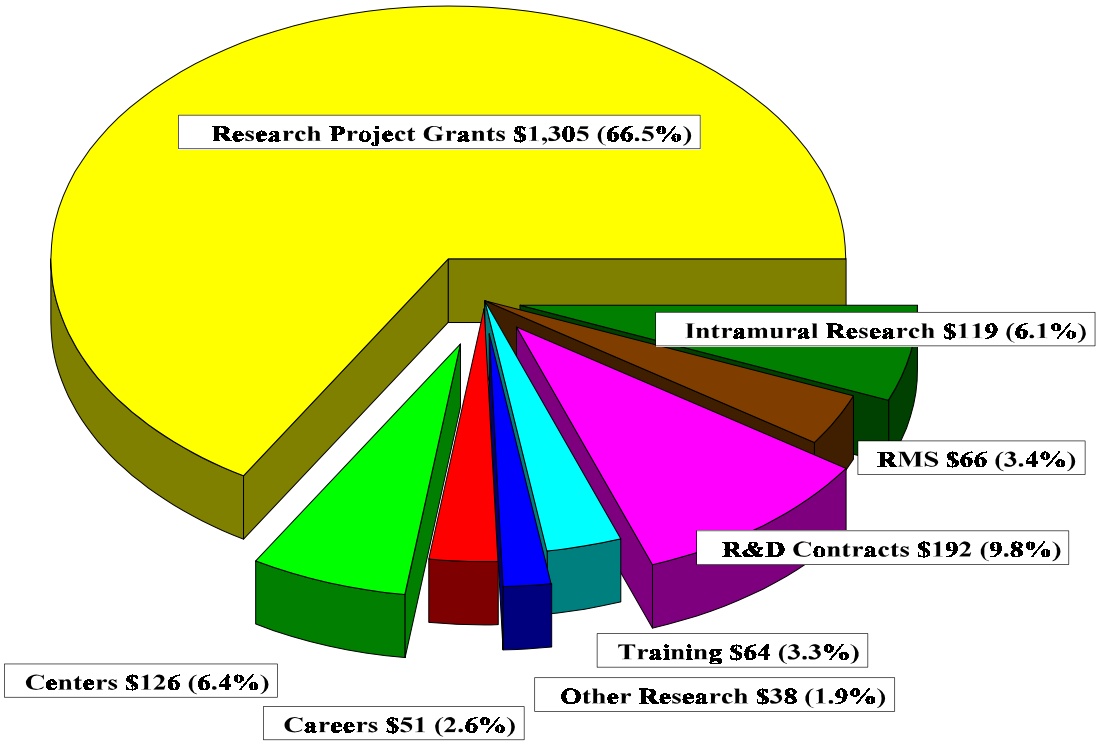
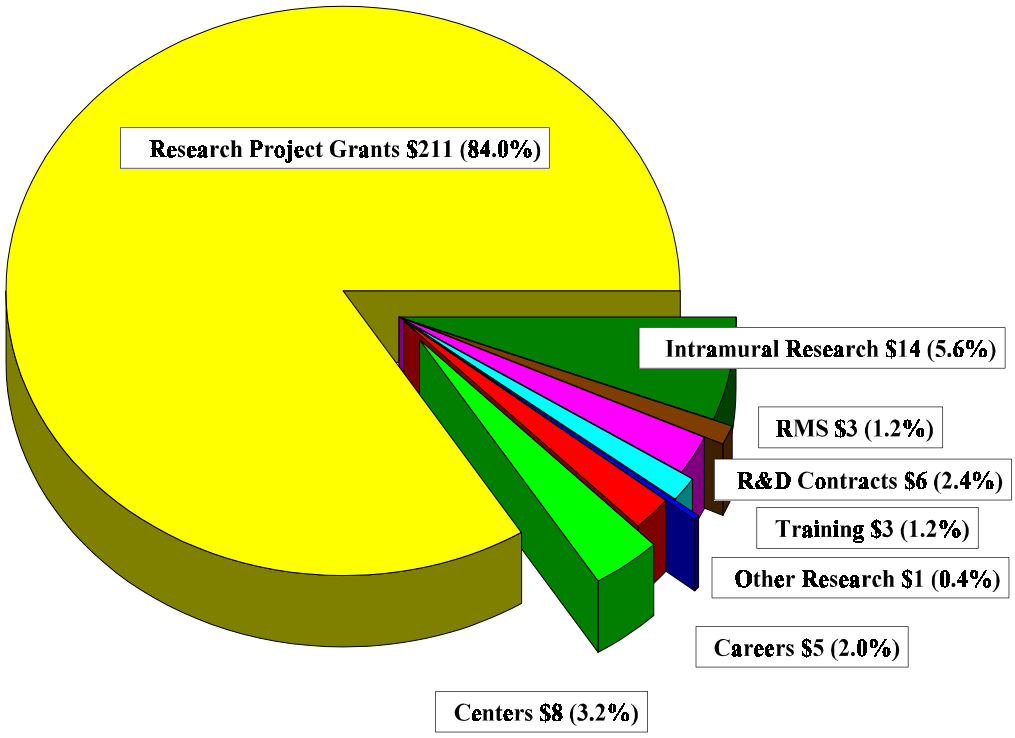
FY 2000 NHLBI Budget By Mechanism

Total = $1,961 million



FY 2000 NHLBI Budget Increase By Mechanism

Increase = $251 million



FY 2000 PLANS

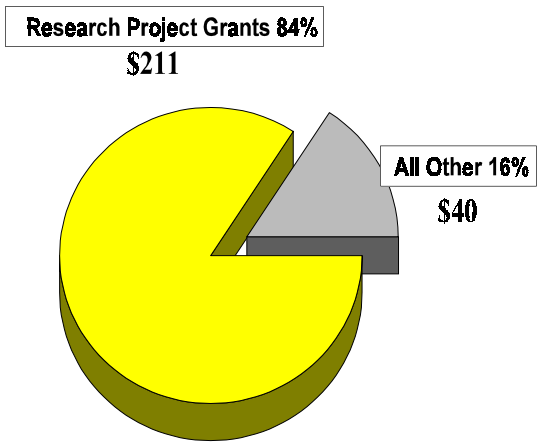
How is the NHLBI spending the FY 2000 budget increase?

The dramatic increases in the NHLBI budget in FY 1999 and FY 2000 have enabled the NHLBI to initiate many new and important basic and clinical research programs, some of which are highlighted in the following pages. An increased investment in medical research continues to provide enormous benefits in the form of new knowledge, new treatments, new diagnostics, new preventions, and new interventions to decrease mortality and morbidity, and improve the quality of life for those who suffer from disease and disability. The rate of our progress is directly related to the creativity of our researchers and is only limited by the resources made available to support medical research and the infrastructure that sustains it.

The following charts explain how the FY 2000 funding increase will be spent by research mechanism, accompanied by examples of new and expanded research supported with the FY 2000 increase.

RESEARCH PROJECT GRANTS (RPGS)

Share of the FY 2000 Increase ($ in Millions)



Definition - Research project grants (RPGs) are the most common funding mechanism used by the NHLBI. They are generally initiated by the investigator and used to support scientific research or training. A research grant provides a commitment of support for an average of four years of funding. Thus, after the competing year, the grantee receives noncompeting continuations each year for the specified length of the grant. The bulk of funding allocated to RPGs supports noncompeting continuations that allow important research to continue.

RPG Budget Distribution - FY 2000
84% of the increase
67% of total budget
1,066 competing grants
3,824 total grants (w/SBIR/STTR)
$1,305m = total Research Projects

- **RPG Budget Increase Breakout**
  - $ 124m - To cover increase in number of non-competing RPGs
  - $ 55m - To support an additional 149 competing RPGs
  - $ 26m - To increase the average cost of competing RPGs
  - $ 6m - SBIR/STTR set-aside
  - $ 211m - of the $251m increase

New and Expanded FY 2000 RPG Programs

Heart and Vascular Diseases Program

Cellular and Molecular Mechanisms of Diabetic Cardiomyopathy – new Request for Applications (RFA) to evaluate the molecular and cellular mechanisms that underlie the pathogenic processes that lead to cardiomyopathy in diabetic patients. The aim is to understand the basic genetic, molecular, and cellular processes responsible for the observed pathophysiology of diabetic cardiomyopathy and ultimately discover new interventions that effectively reverse or prevent disease progression.

Electrical Remodeling: Novel Opportunities for Arrhythmia Control – new RFA to elucidate the mechanisms responsible for the functional, molecular, and structural myocardial changes attributable to electrical remodeling and leading to arrhythmias. Studies are sought that focus on cellular and molecular mechanisms, genetic susceptibility, pharmacologic intervention, identification of populations at risk, and development of novel strategies to prevent progression and recurrence of arrhythmias. The overall goal is to stimulate innovative multidisciplinary research to develop new strategies for the treatment of arrhythmias causing high rates of morbidity and mortality.

Genetic Determinants of High Blood Pressure: Research Networks (aka Family Blood Pressure Program) – renewal of RFA to continue the networks established in 1995 to encourage research collaborations to use modern molecular genetic tools to map and identify the major genetic determinants of high blood pressure. The networks also study interactions between genetic and non-genetic determinants of hypertension in defined populations.

Protease Inhibitor Related Atherosclerosis in HIV Infection - new RFA to elucidate, through interdisciplinary and collaborative research, the mechanisms underlying the observed atherosclerotic and diabetes-related side effects of treating HIV-positive patients with protease inhibitor drugs. Studies should address the metabolic and hormonal alterations leading to abnormally high cholesterol and triglyceride levels, altered body fat distribution, and insulin resistance, as well as the relationship between the development of these abnormal metabolic processes and the accelerated progression of atherosclerosis. Collaborative groups should include either two or three research R01 projects consisting of basic science and clinical studies with a common theme.

Trial of Activity for Adolescent Girls (TAAG) - new RFA to test the effectiveness of a coordinated school- and community-based multi-component intervention to prevent the decline in physical activity commonly observed in middle school girls. A multicenter randomized field trial will test an intervention in a multi-ethnic target group. Schools and existing community agencies will provide skills building, supportive environments, and opportunities for participation in physical activity both in and outside of school to improve cardiorespiratory fitness. The seven-year study will involve 15 intervention and 15 comparison middle school-community agency catchment areas with 120 to 140 sixth grade girls each, for a total of approximately 4,000 girls from five different urban/suburban geographic locations. The interventions will be implemented for two years during the seventh and eighth grades. The two primary outcome measures will be cardiorespiratory fitness and self-reported levels of participation in moderate and vigorous physical activity in and outside of school.

Lung Diseases Program

Cellular and Molecular Mechanisms of Primary Pulmonary Hypertension (PPH) - renewal of Program Announcement (PA) to continue important research in primary pulmonary hypertension (PPH) with the emphasis on a mechanistic understanding of the disease. Further studies are encouraged that address, at the cellular and molecular level, mechanisms involved in pulmonary vascular remodeling, pulmonary vascular tone, and the genetic basis of PPH. Priority will be given to research to identify novel genes or vasoactive mediators important in PPH pathology and determine of their functional effects on pulmonary vascular cells, on extracellular matrix, and on pulmonary vascular tone. Further, research integrating the relationship between mediators of vasoconstriction and pulmonary vascular remodeling is strongly encouraged. The ultimate goal is to develop new and effective therapies.

Inflammation in the Pathogenesis of Chronic Obstructive Pulmonary Disease (COPD) - new RFA to define the potential role of inflammatory and immune mechanisms in the development and progression of COPD. This includes initiating events, regulatory mechanisms, and subsequent underlying cellular and molecular processes that lead to inflammation, tissue damage, and remodeling. These insights may lead to a better understanding of the pathogenic mechanisms of COPD and provide a basis for the development of therapeutic modalities specific to COPD as distinguished from other obstructive pulmonary diseases.

Nocturnal Asthma, Chronobiology, and Sleep - new RFA to conduct studies on the pathogenesis of nocturnal asthma and the roles of circadian rhythms, sleep, and sleep disturbances in this disease process. The overall goal is to establish the cellular and molecular mechanisms which underlie the chronobiology of nocturnal exacerbations of asthma and airway inflammation, as well as the roles played by sleep and sleep disturbances. The RFA strongly encourages scientific collaboration among investigators with interests in asthma, chronobiology, sleep medicine, immunology, physiology, and neurophysiology.

Positional Candidate Gene Approaches in Asthma Gene Discovery - new RFA to employ traditional and novel positional candidate gene approaches to identify the gene or genes in a particular chromosomal region that are linked to asthma or asthma-associated phenotypes. Understanding the genetic mechanisms responsible for asthma and allergy may lead to a better understanding of the pathogenesis of asthma, improved preventive measures, and new therapeutic approaches.

Blood Diseases and Resources Program

In Vitro Inactivation of Viruses in Blood Components - renewal of RFA to encourage basic and applied research on the development and evaluation of simple, cost-effective inactivation procedures to destroy the infectivity of transfusion-transmitted viruses in blood components while maintaining the therapeutic effectiveness of these preparations. Possible approaches to be considered under this renewal of an initiative that began in 1995 include viral adherence to affinity columns; use of monoclonal antibodies for *in vitro* neutralization; absorption-filtration procedures; centrifugal removal of viruses; and use of filters for leukodepletion. Applicants must delineate a research plan that focuses on completing a Phase I clinical trial for safety and pharmacokinetics during the final year of the project.

Thalassemia (Cooley's Anemia) Clinical Research Network - new RFA to establish a network of clinical centers with thalassemia major (Cooley's anemia) patients to study the effectiveness of specific interventions that may reduce morbidity and mortality. The network will enhance progress in moving effective therapies, e.g., fetal hemoglobin enhancing agents, gene therapy, or iron chelation, from the laboratory to the bedside through rapid and systematic collaborative testing in phase II and phase III clinical trials. A data coordinating center and five or six clinical centers will be established and poised to begin clinical studies as promising interventions are identified.

Trans-NHLBI

Development of Mouse Phenotypic Screens for Heart, Lung, and Blood Diseases - new RFA to develop new methods of characterizing the observable physiological traits (phenotypes) of mice in order to accelerate the pace at which accurate, reproducible animal models of human, heritable, heart, lung, blood, and sleep diseases are made available to the research community. The initiative will provide support to investigators to (1) develop high volume (5,000 to 20,000 mice per year) screening and characterization protocols; (2) provide for the validation of these screening protocols against normal and genetically-altered inbred mouse strains that approximate the disease of interest; (3) provide for the timely dissemination of information and methodologies to the scientific community; and (4) where necessary, share resources by providing facilities, services, or training to other investigators needing to characterize genetically altered mice.

Genomic Applications for Heart, Lung, and Blood Research - new RFA to establish up to ten Programs for Genomic Applications (PGAs) for Heart, Lung, and Blood Research. The goal of the PGAs is to link, on a genomic scale, the resources and tools of the Human Genome Project (HGP) to major biological processes and systems involved in cardiovascular, pulmonary, hematologic, and sleep function and dysfunction. Candidate functions include development, differentiation, inflammation, vascular biology, and hemostatic mechanisms, while candidate dysfunctions include stroke, heart failure, hypertension, atherosclerosis, arrhythmia, asthma, chronic obstructive pulmonary disease, pulmonary hypertension, sleep disorders, hemoglobinopathies, and thrombotic disorders. The PGAs will identify subsets of genes that are particularly relevant to the biology, diagnosis, management, treatment, and prevention of heart, lung, blood, and sleep-related disorders and prioritize the information for further focused study. The generation and interpretation of data from the PGAs will enable a broad range of investigators to exploit the unique opportunities provided by the information coming from the HGP and related technologies. In addition, the PGAs will establish training and education programs for NHLBI-supported investigators in the use of genomic information and technologies. The ten PGAs are expected to collaborate to develop common protocols, standard procedures, and non-redundant education and training efforts. The award mechanism will be a four-year U01 cooperative agreement grant with the possibility of one four-year competitive renewal.

Oxygen Sensing During Intermittent Hypoxia - new RFA to improve our understanding of how intermittent hypoxia contributes to the pathophysiology of cardiopulmonary, vascular, hematological, and sleep disorders. Intermittent hypoxia is defined as repetitive episodes, lasting up to two minutes, of reduced oxygen supply to tissue that is below physiological levels despite adequate perfusion of the tissue by blood. One objective of the RFA is to determine the basic molecular and genomic processes involved in the cellular response to the hypoxic episodes, including cellular mechanisms that are responsible for the detection and signaling of oxygen level changes. A second objective is to determine the processes mediating adaptive changes in metabolism, oxygen sensing, and gene expression.

Programs of Excellence in Gene Therapy (PEGT) - new RFA to establish up to five multidisciplinary, collaborative research environments that promote the rapid translation of basic, preclinical studies of gene therapy for cardiovascular, pulmonary, and/or hematologic diseases into human pilot experiments. The five-year awards, using the U01 cooperative agreement grant mechanism, will provide shared access to specialized services such as preclinical toxicology testing, generation of vectors for preclinical and clinical use, large scale production of biological reagents (e.g., cytokines), and biostatistical support. In addition, the programs will provide training to NHLBI-supported physician-scientists in translational

(basic science to clinical application) research for gene therapy. Each program will have a minimum of two clinical projects underway at any one time and four to six training positions. One PEGT will serve as the Coordinating Center and Data Core. A one-time competitive renewal for the existing awardees may be awarded for an additional five years.

Trans-NIH

Academic Research Enhancement Award (AREA) - renewal of PA to stimulate research in educational institutions that provide baccalaureate training for significant numbers of research scientists but that have not been major recipients of NIH support. AREA (R15) funds are intended to support new and health-related research projects proposed by faculty members of eligible institutions. An institution is eligible if it has received less than $2 million per year in NIH support in each of four or more of the last seven years. Qualified scientists will receive support for small-scale research projects, such as those that would provide preliminary data for traditional research project grants. The awards are intended to create research opportunities for scientists and institutions otherwise unlikely to participate in NIH programs.

Biobehavioral Pain Research - renewal of PA to stimulate and foster a wide range of basic and clinical studies on pain. Applications are encouraged to study individual differences in pain responses that may be due to such varied factors as genetics, endocrinology, neural activity, immune function, psychological state, disability, age, gender, or cultural background. Research is also needed to understand the neuroanatomical pathways and the neurophysiological mechanisms involved in pain. Studies are encouraged at the level of the gene, molecule, cell, organ, and individual – with the goal of ultimately developing biobehavioral interventions to manage or prevent pain.

Biobehavioral Research for Effective Sleep - new PA to stimulate applied research on behavioral, psychosocial, and physiological consequences of acute and chronic partial sleep deprivation (apart from that caused by any sleep pathology) in either chronically ill or healthy individuals. The research is expected to lead to the development of environmental, clinical, and other interventions to reduce sleep disturbances and significantly improve the health of large numbers of people.

Bioengineering Nanotechnology Initiative - new PA to support Small Business Innovation Research (SBIR) projects on nanotechnologies useful to biomedicine. Nanotechnology is defined as the creation of functional materials, devices, and systems through control of matter at the scale of 1 to 100 nanometers (one-billionth of a meter). The announcement encourages team approaches to create a synergistic blend of expertise and resources involving the commercial, academic, and other sectors of the research community, including engineering, chemistry, physics, materials science, engineering, and biology. Phase I projects will be considered for periods of up to 2 years and total costs of up to $400,000. Phase II projects will be considered for up to 3 years and total costs of up to $1.2 million. The announcement will remain in effect for three years.

Bioengineering Research Grants and Partnerships - new PA to support basic bioengineering studies that are likely to advance health or health-related research within the mission of the NIH. Bioengineering integrates physical, chemical, mathematical, and engineering principles to develop innovative biologics, materials, processes, implants, devices, and informatics for the prevention, diagnosis, and treatment of disease, for patient rehabilitation, and for improving health. The bioengineering research grants will apply basic design-directed or hypothesis-driven bioengineering research to important medical or

biological research areas. The bioengineering research partnerships will support interdisciplinary groups of partners who work together to apply integrative, multidisciplinary, systems approaches to significant areas of basic bioengineering research.

Biology of Iron Overload and New Approaches to Therapy - new RFA to develop a better understanding of the pathogenesis and biological consequences of, and new therapies for, iron overload. A major aspect of this initiative is to elucidate the control of iron transport and metabolism in order to facilitate the development of improved means of removing excess iron.

Bone and the Hematopoietic and Immune Systems - new PA to elucidate the functional interactions between bone and the hematopoietic and immune systems. Recent observations underscore the linkage between endochondral bone formation and the establishment of hematopoietic marrow and suggest that interactions between bone, marrow, and the immune system persist in the mature skeleton. In order to explore the mechanisms that underlie these interactions, the participating Institutes will support projects that have the potential to either clarify the importance of specific cell types and effector molecules or identify previously unrecognized cellular and molecular agents that influence bone physiology. Collaborations are encouraged among bone biologists, hematologists, and immunologists, and between basic scientists and clinical investigators.

Impact of Aging on Development of Atrial Fibrillation - new PA to enhance our understanding of age-related structural and functional changes in the atria and their impact on the development of atrial fibrillation (AF) in older persons. This joint program announcement with the National Institute on Aging is intended to foster integrative, clinically-related research incorporating the tools of molecular and cell biology for the study of function and clinical outcomes. The long-term goal of the program is to provide the groundwork for the primary prevention of AF.

Mechanisms in Immuno-Modulation Trials: Hyper-Accelerated Awards - new RFA to conduct mechanistic studies in clinical trials of immuno-modulatory interventions for immune-system-mediated diseases, including asthma and allergy, graft failure in solid organ and stem cell transplantation, and autoimmune diseases. Specifically, the RFA focuses on the utilization of patients and patient materials from such trials for the evaluation of immunologic and other relevant parameters in order to study the mechanisms underlying the intervention, the mechanisms of disease pathogenesis, surrogate markers of disease activity and therapeutic effect, and mechanisms of human immunologic function. The parent or core clinical trial must have independent financial support and will not receive support under this RFA. Mechanistic studies in clinical trials supported by industry are particularly encouraged. In order to avoid delay of the parent or core clinical trial, applications will be subject to a hyper-accelerated review process under which awards will be made thirteen weeks after the application receipt date.

Mechanisms Underlying Individual Variations in Drug Responses - new PA to identify the critical candidate proteins and genes that play essential roles in determining individual variations in drug responses. The study of pharmacogenetic and pharmacogenomic variation presents opportunities for researchers, working at levels ranging from the most molecular to the most clinical, in the fields of pharmacology, genetics, genomics, medicine, epidemiology, statistics, and computer science. The announcement is one of a pair of trans-NIH initiatives, led by the National Institute of General Medical Sciences, designed to address the collection of fundamental knowledge required to predict individual differences in drug responses. The companion solicitation will create a common, public pharmacogenetic database. Awardees from this announcement should plan to deposit sequence, function,

and phenotype information into the pharmacogenetic database as it is developed. The NHLBI is specifically interested in studies of drug response proteins and genes involved in cardiovascular, pulmonary, and hematologic systems.

Microbial Biofilms: Study and Control (SBIR/STTR) - new PA to develop technologies and strategies for the prevention and treatment of microbial biofilm-associated diseases. A biofilm is an accumulation of microorganisms (bacteria, fungi, and/or protozoa, with associated bacteriophages and other viruses) embedded in a polysaccharide matrix and adherent to a solid biologic or non-biologic surface. Biofilms, accounting for over 80 percent of microbial infections in the body, tend to be far more resistant to antimicrobial agents and to be particularly difficult for the host immune system to respond to appropriately. Under the auspices of the Small Business Innovation Research (SBIR) Program and the Small Business Technology Transfer (STTR) Program, this initiative is intended to integrate current research in immunology, microbiology, bio-engineering and computer technology with current biofilm research. It is also intended to link clinical experts, e.g., nurses, physicians, respiratory therapists, and orthopedic technicians, with bioengineers and basic scientists to identify clinical problems associated with microbial biofilm-associated infection.

Mouse Mutagenesis And Phenotyping: Developmental Defects - new RFA to establish a facility for large-scale mutagenesis and phenotyping of developmental defects in the laboratory mouse. The immediate objective of the facility is to produce and characterize mouse strains harboring mutations that affect normal developmental processes. Ultimately, the mutant mice produced in this facility are expected to help elucidate the basic cellular, molecular, and genetic mechanisms that direct embryonic and post-embryonic growth and function, as well as yield insights into the mechanisms of human disease. It is anticipated that the facility will devise and perform efficient genome-wide mutagenesis, devise and perform high-throughput phenotyping to screen for mutations that disrupt normal developmental processes, and devise and perform detailed characterization of mutants that display defects in development. Mutant mice, protocols, assays, assessment criteria, and other materials and information generated in projects funded under the RFA will be made available to the wider biomedical community.

Pharmacogenetic Research Network and Database - new RFA to establish a series of multidisciplinary, collaborative research groups to study how genetic variation contributes to inter-individual differences in drug responses and to collect comprehensive, integrative information about specific response-related proteins and genes. A database group will also be established for design and implementation of a pharmacogenetic database. All groups will be expected to work cooperatively so that the pharmacogenetic database will become an information resource that is of maximum utility to the entire research community and can stimulate future hypothesis-driven research. Nine groups were funded NIH-wide to begin in FY 2000 and an additional two to four groups are expected to be funded to begin in FY 2001. In FY 2000, the NHLBI supported a multi-center group to discover which genes play a role in people's widely variable responses to the three main types of asthma treatments..

Protein Structure Initiative (Structural Genomics) -- SBIR/STTR - new PA to encourage small business concerns to develop methodologies and technologies to support the emerging field of structural genomics, whose goal is to understand protein structural families, structural folds, and the relation between protein structure and function. Projects related to high throughput structure determination by x-ray crystallography and NMR, as well as those addressing other constituent tasks of structural genomics, are relevant to this trans-NIH program announcement. Support for the program is through the Small

Business Innovation Research (SBIR) Program and the Small Business Technology Transfer (STTR) Program.

Research on Hematologic Abnormalities in AIDS - renewal of PA to study the cellular basis of hematologic abnormalities that are common in AIDS patients and significantly affect their course of treatment. Examples of target conditions include bone marrow dysplasia, anemia, thrombocytopenia, and leukopenia. Studies of retroviral-induced neoplasms of immunodeficiency states are expected to provide useful information about the cellular and humoral bases of immune responses, including the mechanisms leading to hematologic abnormalities that are seen following HIV infection.

Stem Cell Research: Novel Approaches To Enhance - new PA to enhance stem cells as models for the study of biological and disease processes. This trans-NIH initiative supports research to isolate, characterize, and identify stem cells that are totipotent (those that give rise to all cells) and multipotent (those that give rise to all cells performing a particular function) from animal models and to generate reagents and techniques to characterize and separate them from other cell types. The initiative stresses innovative approaches to the problems of making multipotent stem cells available from a variety of nonhuman sources, and of creating reagents that will identify those stem cells across species and allow for separation of multipotent stem cells from differentiated cell types.

Technologies to Improve the Utility of Animal Models - new PA to encourage the small business community to develop technologies, reagents, and equipment to improve the utility of animal models for biomedical research. Projects supported under this PA are expected to improve laboratory animal welfare, improve long-term maintenance and preservation of laboratory animal models, and improve technologies for the generation of animal models of human disease. The NHLBI has an interest in the generation of new animal models of cardiovascular diseases that closely simulate human cardiovascular diseases in order to investigate the molecular mechanisms underlying normal and abnormal development, physiology, and pathophysiology of the cardiovascular system. In addition, development of new methods to measure essential cardiovascular performance parameters, such as heart wall motion and coronary blood flow, especially in small animal models, such as mice, is desired. Applicants follow all relevant procedures of the PHS Small Business Innovation Research (SBIR) Program and the NIH Small Business Technology Transfer (STTR) Program.

Testing Interventions to Improve Adherence to Pharmacological Treatment Regimens - new RFA to encourage behavioral and social research on the effectiveness of interventions to improve adherence to therapeutic regimens in various settings. Therapeutic regimens must include a pharmacological treatment that has been demonstrated to be efficacious for an existing illness or condition. Adherence interventions must target individuals, formal or informal health-care providers, and/or the social or institutional environment, and measurements must be available of both the delivery (i.e., treatment fidelity) and adherence to the regimen. Applicants are encouraged to investigate how to adjust interventions to take into account the characteristics of different populations as well as people suffering from, and receiving treatments for, multiple acute and/or chronic illnesses and conditions. The NHLBI is especially interested in the following therapies and conditions where adherence poses special problems: antihypertensive therapies, cholesterol-lowering medications, medications used to treat myocardial infarction and congestive heart failure, and treatments for asthma, tuberculosis, and sickle cell disease.

Therapeutic Modulation of Angiogenesis in Disease - new PA with Review to translate current laboratory-based knowledge of angiogenesis (the process by which new blood vessels arise as outgrowths

of existing vessels) into therapeutic applications for addressing a wide range of cardiovascular and pulmonary diseases, for inhibiting tumor growth and metastasis, and for treating certain eye diseases. This NIH-wide program announcement, with review by a special emphasis panel, encourages testing of known pro- and anti-angiogenic agents in appropriate model systems unique to a particular disease. The results would be translated to the clinical arena as potential treatment modalities. In a number of cases, where the appropriate models may not exist for testing these agents or for predicting clinical outcome, the models will need to be developed.

Thrombosis of the Arterial and Cerebral Vasculature: New Molecular Genetic Concepts for Prevention and Treatment - new RFA to establish collaborative teams of closely interacting investigators with diverse, complementary areas of expertise to elucidate the molecular genetic mechanisms of thrombosis in the arterial and cerebral vasculature. The overall goal is to stimulate innovative multidisciplinary research to expedite progress in understanding the pathogenesis of thrombosis in the arterial and cerebral vasculature and to facilitate the application of new findings for better detection, prevention, and treatment. The initiative will support research to map and identify genes that confer susceptibility to or protection from thrombosis in the arterial and cerebral vasculature, to perform mechanistic studies that will clarify the role of specific genetic alterations that lead to or help prevent organ specific thrombosis, and to apply and further refine sophisticated molecular genetic methods and technologies, such as DNA arrays, gene knock-outs, gene knock-ins, and gene alterations directed to specific tissues at specific times in development.

Trans-PHS

Ethical Issues in Human Studies - new PA to conduct research on ethical issues that arise with research involving human participants in order to guide researchers and Institutional Review Board (IRB) members towards promoting appropriate protections for research participants. Topics of interest include: how best to provide information about a study's methods and procedures to improve participants' comprehension, the effect of different recruitment strategies on retention of study participants, and the effects of investigator characteristics and behavior on levels of recruitment, retention, and withdrawal. Also relevant are conflicts of interest, perilous procedures or interventions, inducements to participation, risks and benefits of deciding to consent or refuse, justice in the selection of participants, consequences of withdrawal from a study, exceptions to privacy and confidentiality, uses of collected tissues or cells, uses of collected data, cognitive ability required to consent, the concept of “community” in the context of research, the impact on participation of monetary incentives on varied socioeconomic groups, social harms, medical records issues, the ethical design and conduct of cross-cultural studies, and monitoring protocol review.

National Occupational Research Agenda (NORA) Implementation - renewal of RFA to develop knowledge that can be used in preventing occupational diseases and injuries and to better understand their underlying pathophysiology. The following types of applied research projects will be supported under this trans-PHS (CDC and NIH) RFA: causal research to identify and investigate the relationships between hazardous working conditions and associated occupational disease and injury; the nature and magnitude of special risk factors experienced by older and/or minority workers; methods research to develop more sensitive means of evaluating hazards at work sites; and evaluations of the effectiveness of prevention and intervention programs, including new approaches or combinations of techniques such as control technologies, personal protective equipment, and changes in work organization factors. The

NHLBI is especially interested in asthma, chronic obstructive pulmonary disease, and sleep disorders, as they relate to occupational health.

Interagency

Beryllium-Induced Diseases - new PA to understand the cellular and molecular events that underlie the transition from antigen sensitization to beryllium to chronic beryllium disease. The goal of this research is to improve the identification of markers of disease initiation and progression in order to develop early therapeutic interventions and effective environmental control strategies. Although beryllium is a naturally occurring substance, the major source of its emission into the environment is the combustion of fossil fuels, primarily coal, which releases beryllium-containing particulates and fly ash into the atmosphere. The most significant exposure to beryllium occurs in the occupational setting. Workers potentially exposed are those engaged in primary production, metal machining, and reclaiming scrap alloys. In chronic disease, the alveoli contain small interstitial granulomata that resemble those seen in sarcoidosis. As the disease progresses, the granulomas become organized and eventually form small, fibrous nodules resulting in progressive impairment of pulmonary function.

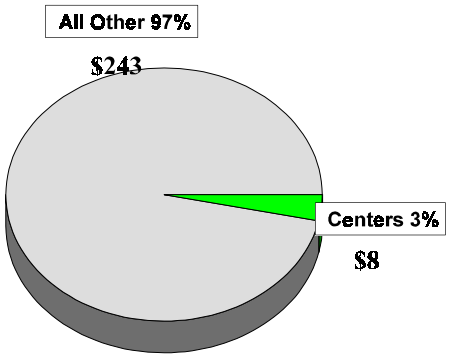
Earth-Based Research Relevant to the Space Environment - new PA to stimulate Earth-based research on basic, applied, and clinical biomedical and behavioral problems that are relevant to human space flight or that could use the space environment as a laboratory. Potential areas of research of interest to the NHLBI include pulmonary function, immunology, cardiovascular functioning, hemodynamics, and sleep and biological rhythms. Use of hyper- or hypo-gravity, as research tools or models, is encouraged, and access to NASA facilities can be provided. Although none of the research supported under this initiative would be conducted in space, it is anticipated that it would form a basis for future competitively reviewed studies which could be conducted on the International Space Station, or other space flight opportunities, by skilled on-board specialists.

Human Brain Project (Neuroinformatics): Phase I & Phase II - renewal of PA to develop new digital and electronic neuroinformatic tools for all domains of neuroscience research. Neuroinformatics combines neuroscience and informatics research to develop and apply advanced tools and approaches essential for understanding the structure and function of the brain. Research in informatics includes databases, graphical interfaces, querying approaches, information retrieval, data visualization and manipulation, data integration through the development of integrated analytical tools, synthesis, and tools for electronic collaboration. In computational research, the focus is on development of structural, functional, integrative, and analytical models and simulations. This program announcement supports Phase I and Phase II projects in a three-phase process. Phase I projects consist of research feasibility studies. Phase II projects consist of expanded beta testing, further refinement of newly developed tools, and the development of appropriate models and simulation capabilities. The tools resulting from this research and development will be made available to the scientific community at large in Phase III.

Neuroinformatics: Short Courses - new PA with Review to develop short courses, seminars, and workshops in interdisciplinary neuroinformatics education for scientists seeking to combine expertise in informatics research with knowledge about the various subdisciplines of neuroscience and behavioral science. These short courses will allow the participants to: (a) acquire new conceptual approaches to basic neuroscience research and analyses; and (b) develop unique strategies for acquiring, storing, retrieving, organizing, managing, analyzing, visualizing, manipulating, integrating, synthesizing, disseminating, and sharing data about the brain and behavior. Each project will be identified as a unit of, and be linked to the web site of, the NIH/NSF/DOE Human Brain Project/Neuroinformatics program at http://www.nimh.nih.gov/neuroinformatics/index.cfm.

CENTERS

Share of the FY 2000 Increase ($ in Millions)



Definition - Research Center grants are awarded to extramural research institutions to provide support for long-term, multi-disciplinary programs of medical research. They support development of research resources to aid in integrating basic research with applied research and transfer activities. Finally, they promote research on clinical applications emphasizing prototype development and refinement of products, techniques, processes, methods, and practices.

Centers Budget Distribution - FY 2000
3% of the increase
6% of total budget
85 centers
$126m = total Research Centers

- **Centers Budget Increase Breakout**
  - $ 3m - To support Ischemic Heart Disease in Blacks
  - $ 5m - To support Hematopoietic Stem Cell Biology
  - $ 8m - of the $251m increase

New and Expanded FY 2000 Centers Programs

Heart and Vascular Diseases Program

Specialized Centers of Research (SCORs) in Ischemic Heart Disease in Blacks - renewal of RFA to advance our understanding of the expression of ischemic heart disease in blacks through the application of modern methods and approaches to molecular biology, cellular and organ physiology, and clinical practice. Applicants should select one of three themes: sudden cardiac death, microvascular disease, or diabetic heart disease, as the focus of their applications. Interdisciplinary and collaborative studies are encouraged on the efficacy and mechanisms of complementary and alternative medicine (CAM) in the context of this RFA. The specific CAMs acceptable for inclusion are phytotherapy or herbalism (e.g., ginkgo biloba, garlic, Hawthorne); orthomolecular medicine (e.g., nutritional and food supplements used in combinations and at very high doses); and mind-body medicine as used in the black population. This open SCOR competition is for the second of two five-year periods of support, the first being for fiscal years 1995 to 1999.

Specialized Centers of Research (SCORs) in Ischemic Heart Disease, Sudden Cardiac Death, and Heart Failure - renewal of RFA to establish specialized centers of interdisciplinary and collaborative research on the etiology, pathophysiology, diagnosis, and treatment of ischemic heart disease, sudden cardiac death, and heart failure. A center should have a main theme to which all of its sub-projects pertain and should be integrated in such a way as to translate research findings into the clinical setting. Applications must include sub-projects in both basic and clinical science and must include patient studies. The goals of the program are to (1) exploit the latest techniques of genetic and molecular biology, and cellular and organ physiology, to elucidate the underlying mechanisms that are perturbed in cardiac disease states; and (2) apply fundamental knowledge and modern technology to improve the diagnosis, treatment, and prevention of these diseases. Core units may be included to provide services to the various research sub-projects and to support the organizational and administrative aspects of the center. This program will also support studies on the efficacy and mechanisms of complementary and alternative medicine for treating the subject diseases, but will be limited to studies of phytotherapy or herbalism (e.g., gingko biloba, garlic, Hawthorne) and orthomolecular medicine (i.e., nutritional and food supplements used for therapeutic or preventive purposes, usually in combinations and at high doses.)

Blood Diseases and Resources Program

Specialized Centers of Research (SCOR) in Hematopoietic Stem Cell Biology - renewal of RFA to extend for a second five-year period the SCOR program to advance our knowledge of basic stem cell biology in areas of stem cell isolation, quantitation by *in vivo* assay, *in vitro* and *in vivo* growth and expansion, gene insertion and long-term expression, and engraftment. This basic knowledge will be applied clinically to enhance our ability to achieve hematopoietic stem cell therapy that cures both genetic and acquired diseases and to perform successful gene therapy using the hematopoietic stem cell as the target for gene transfection and for life-long expression of normal genes. The SCOR mechanism is uniquely designed to support a spectrum of multidisciplinary basic and clinical research in a synergistic fashion so that major therapeutic advances will be realized in the next decade in both gene therapy and stem cell transplantation.

Trans-NIH

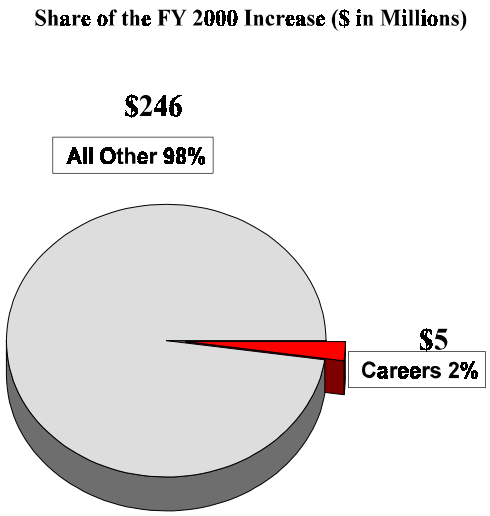
Centers for AIDS Research (CFARs) - new PA with Review to support center core grants that provide infrastructure and promote basic, clinical, behavioral, and translational AIDS research activities at institutions that receive significant AIDS funding from multiple NIH Institutes or Centers. CFARs foster synergy and improve coordination of research, support emerging research opportunities, and promote economies of scale through the sharing of resources by multiple independent laboratories.

Centers for Complementary and Alternative Medicine Research - renewal of RFA to examine the potential efficacy, effectiveness, safety, and validity of complementary and alternative medicine (CAM) practices, as well as the physiological or psychological mechanisms underlying these practices. This trans-NIH initiative will use the Specialized Centers of Research (P50) grant mechanism. Research theme areas of interest to the NHLBI include asthma (in 1999 and 2000) and sleep disorders (in 1999). For asthma, interventions of interest include hypnotic suggestion, acupuncture, homeopathy, salt reduction and magnesium supplementation, herbal remedies, Ayurvedic medicine, and breathing techniques. For sleep disorders, interventions of interest include light, food supplements, exercise, and unconventional pharmacological, herbal and orthomolecular interventions. Each center is required to

have an administrative core, three to six sub-projects, a program of short-term developmental and feasibility projects, a career development program, and an advisory committee. This program began with 8 centers in 1999 and is adding 3 additional centers in 2000.

Centers For Dietary Supplements Research: Botanicals - renewal of RFA to establish Specialized Research Centers to investigate the biological effects of botanicals including, but not limited to, botanicals available as dietary supplements. The creation of such Centers is needed to advance the quality and quantity of scientific information on botanicals and to promote further research in this area. It is anticipated that a fully integrated Center eventually will have the capacity to (1) identify, characterize, and authenticate botanicals, (2) assess the bioavailability and bioactivity of botanical ingredients, (3) identify active constituents in botanicals and explore their mechanism(s) of action, and (4) conduct both pre-clinical and clinical evaluations of botanicals. Botanicals of interest to the NHLBI include those that influence risk factors for atherosclerosis such as insulin resistance, dyslipidemia, hypertension, and central obesity; those that interact with vascular cells; those that influence blood vessel spasms, contraction, or dilation; and those that influence the coagulation cascade and various proteins and factors of thrombosis.

CAREERS



Definition

Research Career Programs (K awards) -Designed to provide increased career opportunities in medical research to scientists of superior potential. The programs provide support for young investigators who desire advanced development and scientists who need experience to qualify for senior positions. Included within this category are the following awards: Research Career Development Awards, Clinical Investigator Awards, Academic Awards, Career Transition Awards, Special Emphasis Research Career Awards, and Physician/Scientist Development Awards.

Careers Budget Distribution - FY 2000
2% of the increase
3% of total budget
430 careers
$51m = total Research Careers

- **Careers Budget Increase Breakout**
  - $ 3m - To support the Clinical Research for K23, K24, & K30's Awards
  - $ 1m - To support the Nutrition Academic Awards
  - $ 1m - To support the Minority Institution/Faculty Awards
  - $ 5m - of the $251m increase

New and Expanded FY 2000 Careers Programs

Trans-NHLBI

Mentored Minority Faculty Development Award (K01) - renewal of RFA to support under-represented- minority faculty members with varying levels of research experience to prepare them for research careers as independent investigators. This award will enable suitable faculty candidates holding doctoral degrees, such as the Ph.D., M.D., D.O., D.V.M., or an equivalent degree, to undertake three to five years of special study and supervised research under an established-scientist sponsor, competent to provide guidance in the proposed area of research. The objective of the award is to develop highly-

trained minority investigators, whose basic or clinical research interests are grounded in the advanced methods and experimental approaches needed to solve problems related to cardiovascular, pulmonary, and blood diseases, transfusion medicine, and sleep disorders. These minority individuals may serve as role models for minority undergraduate and graduate students and stimulate them to become more cognizant of research opportunities in areas of interest to the NHLBI.

Minority Institution Research Scientist Development Award (K01) - renewal of RFA to enhance research skills in areas relevant to the NHLBI of faculty members with doctoral degrees in biomedical or behavioral science at minority institutions. Applicant faculty members for this award establish a mentoring relationship with an accomplished investigator at a nearby institution and develop a program of up to five years of intensive, full-time, training during the summer periods and part-time (minimum 25 percent) during the academic year. Applicants are responsible for the planning, direction, and execution of their own program and receive funds for salary and research support and for one or two student research assistants. Current and former recipients may apply for a second five-year period of support.

NHLBI Career Transition Award (K22) - new PA with Review to enable outstanding students with three to five years of postdoctoral training to obtain a research training experience in the NHLBI Division of Intramural Research and to facilitate their successful transition to an extramural environment as independent researchers. The award provides up to three years of support for full-time research training in an NHLBI intramural laboratory followed by two years of support for an independent research project (minimum of 75 percent effort) in an extramural institution. It is anticipated that awardees will subsequently obtain research project grants such as R01s to support continuation of their work.

Trans-NIH

Independent Scientist Award (K02) - new PA to provide up to five years of salary support for newly independent scientists who can demonstrate the need for a period of intensive research focus as a means of enhancing their research careers. The award is intended to foster development of outstanding scientists and enable them to expand their potential to make significant contributions to their fields of research. Candidates must have a doctoral degree and independent, peer-reviewed research support at the time an award is made.

Mentored Clinical Scientist Development Award (K08) - new PA to support development of outstanding clinician research scientists by providing specialized study for individuals with a health professional doctoral degree who are committed to a career in laboratory or field-based research. Candidates must have the potential to develop into independent investigators. The award supports a three-, four-, or five-year period of supervised research experience at a minimum of 75 percent effort that integrates didactic studies with laboratory or clinically-based research. The proposed area of investigation must have intrinsic research importance while serving as a suitable vehicle for learning the methodology, theories, and conceptualizations necessary to function as an independent researcher. Candidates must be able to identify a mentor with extensive research experience who has sufficient independent research support to cover the costs of the proposed research project in excess of the allowable costs of this award.

Mentored Patient-Oriented Research Career Development Award (K23) - new PA to support career development of investigators who have made a commitment to focus their research endeavors on patient-oriented research. The announcement offers support for a non-renewable three- to five-year period of

supervised study and research for clinically-trained professionals with the potential to develop into productive investigators who interact directly with human subjects. The proposed areas of research may include mechanisms of human disease, therapeutic interventions, clinical trials, and/or development of new technologies. Candidates must be willing to spend a minimum of 75 percent of full-time professional effort conducting research career development and clinical research. Proposals should be carefully tailored to meet a candidate's individual needs and must include a mentor or mentors who are competent to provide appropriate research guidance. At the completion of the award, candidates should have both the knowledge and the skills necessary to compete for independent research support.

Mentored Quantitative Research Career Development Award - new PA to support career development of investigators with quantitative scientific and engineering backgrounds outside of biology or medicine who have made a commitment to focus their research endeavors on behavioral or biomedical research. The award provides support for a three- to five-year non-renewable period of supervised study and research, entailing at least a 75 percent effort, for research-oriented scientists at the level of junior faculty who have the potential to integrate their expertise with biomedicine and develop into productive, independent investigators. Examples of backgrounds considered appropriate for the award are mathematics, statistics, computer science, informatics, physics, chemistry, and engineering. An active mentor must be chosen who is competent and willing to provide appropriate research guidance.

Midcareer Investigator Award in Patient-Oriented Research (K24) - new PA to allow outstanding clinical scientists an opportunity to engage in patient-oriented research and to act as mentors for beginning clinical investigators. Candidates for the award are investigators with independent research support, who are within 15 years of their specialty training, and can demonstrate the need for a period of intensive research focus as a means of enhancing their clinical research careers. In addition, they should be committed to mentoring the next generation of clinical investigators focusing on patient-oriented research. The 60 to 80 anticipated awards under the announcement, requiring a 25 to 50 percent time effort, are designed to provide partial relief from patient care duties and administrative responsibilities for a period of three to five years.

Nutrition Academic Award - renewal of RFA to encourage development or enhancement of medical school curricula to increase opportunities for students, house staff, faculty, and practicing physicians to learn principles and clinical practice skills of nutrition with an emphasis on preventing cardiovascular diseases, obesity, diabetes, and other chronic diseases. A second objective is to provide training modules for dissemination to other medical schools and the field.

Interagency

Neuroinformatics Institutional Mentored Research Scientist (K12) Development Award - new PA with Review to establish programs in U.S. educational institutions to provide post-doctoral neuroscientists and behavioral scientists with mentored training in informatics and conversely provide post-doctoral informatics scientists with mentored training in neuroscience and behavioral science. Upon completion of this interdisciplinary program, appointees are expected to engage independently in neuroinformatics research to elucidate the etiopathophysiology of mental and neurological disease. Under the award, up to three scientists at a time will begin a well-structured, phased developmental program that includes a designated period of didactic training followed by a period of supervised research experience. The programs would be considered units of the NIH/NSF/DOE Human Brain Project/Neuroinformatics Program.

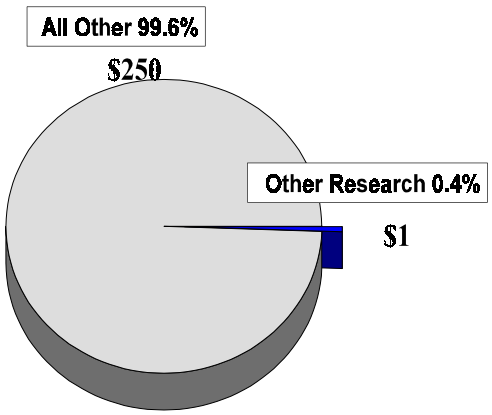
Neuroinformatics Research and Analysis: Curriculum Development (K07) Award - new PA with Review to develop courses and curricula to train interdisciplinary neuroinformatics scientists at U.S. graduate and undergraduate educational institutions to advance our understanding of brain structure and function in health and illness. The field of neuroinformatics combines neuroscience research with informatics research which draws heavily from the fields of computer science, mathematics, physics, and engineering. It is anticipated that these courses or curricula would be useful to students and scientists who wish to: (1) develop new conceptual approaches to basic and/or clinical neuroscientific research and analysis; or (2) acquire, store, retrieve, organize, manage, analyze, visualize, manipulate, integrate, synthesize, disseminate, or share data about the brain and behavior. The courses or curricula will be developed and implemented in the awardee institutions and will serve as models that can be transferred in whole or in part to other institutions. Awards will be from 3 to 5 years in length and are non-renewable. The projects will be considered units of the NIH/NSF/DOE Human Brain Project/Neuroinformatics Program.

Private-Public Partnerships

Transitional Career Development (K22) Award in Women's Health Research - new RFA to support career development experiences leading to independence for clinical investigators interested in patient-oriented or population-based research related to diseases or medical conditions that occur with higher prevalence in women. The award provides an opportunity for investigators to develop clinical research skills during two years of study and research in the NIH Intramural Research Program. It also includes a follow-on two-year period of salary and research support at an academic institution of the candidate's choice.

OTHER RESEARCH PROGRAMS

Share of the FY 2000 Increase ($ in Millions)



Definition - Other Research comprises a number of activities, including:

Cooperative Clinical Research - Grants awarded to multiple institutions where investigators are asked to follow common research protocols, because there are insufficient numbers of subjects available at a single institution to conduct a major clinical trial. NHLBI staff are substantially involved in the management of these awards.

Biomedical Research Support (BRS) - Grants awarded to NHLBI-supported institutions to fund shared instrumentation needs.

Minority Biomedical Research Support (MBRS) - Designed to increase the number and quality of ethnic minority biomedical research scientists by strengthening the capability of eligible institutions to conduct quality research in the health sciences and to support undergraduate students in biomedical research at minority institutions.

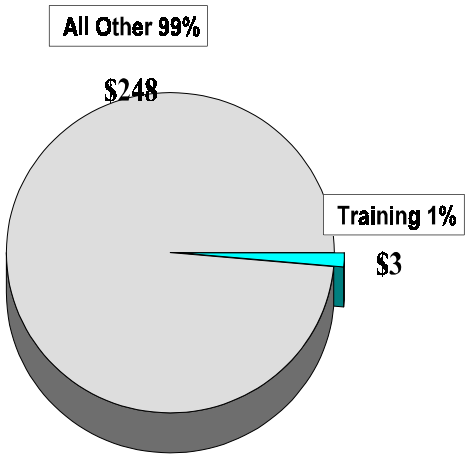
Other Research Related Grants - Various small grants, including scientific review and evaluation, small instrumentation, and conference grants.

Other Research Budget Distribution -FY 2000
0.4% of the increase
2% of total budget
82 other research grants
$38m = total Other Research

- **Other Research Budget Increase Breakout**
  - $ 1m - To increase the number of Other Research awards by 2, and increase support for the Cooperative Clinical Research Support and Minority Biomedical Research Support (MBRS) Programs.
  - $ 1m - of the $251m increase

RESEARCH TRAINING

Share of the FY 2000 Increase ($ in Millions)



Research Training Budget Distribution -FY 2000
1% of the increase
3% of total budget
1,765 NRSAs
$64m = total Research Training

Definition - The National Research Service Awards (NRSA) program serves to replenish the Nation's corps of biomedical and behavioral research investigators. Through institutional awards and individual fellowships, the NHLBI supports both basic and applied research training in the biomedical and behavioral sciences. Institutional awards provide the foundation by supporting the national capacity for excellent, up-to-date training in a variety of settings. They enable the NHLBI to aid institutions in maintaining vigorous and effective research training programs and, in particular, to support research training programs in areas of national need. Decisions on the number of research trainees to be supported by the NHLBI are based upon assessments of program needs and opportunities by the institue, recommendations of the National Academy of Sciences (NAS) and other groups, and the availability of funds.

- **Research Training Budget Increase Breakout**
  - $ 3m - To increase stipends, Health Insurance, and Institution allowances.
  - $ 3m - of the $251m increase

New and Expanded FY 2000 Training Programs

Trans-NHLBI

Short-Term Training for Minority Students (T35M) - renewal of RFA to encourage institutions to provide opportunities for under-represented-minority students at the undergraduate and graduate levels to become exposed to biomedical research in areas relevant to cardiovascular, pulmonary, and hematologic diseases, and sleep disorders, through a short-term full-time research experience of two to three consecutive months. Grantee institutions are responsible for selecting and appointing trainees. Four to

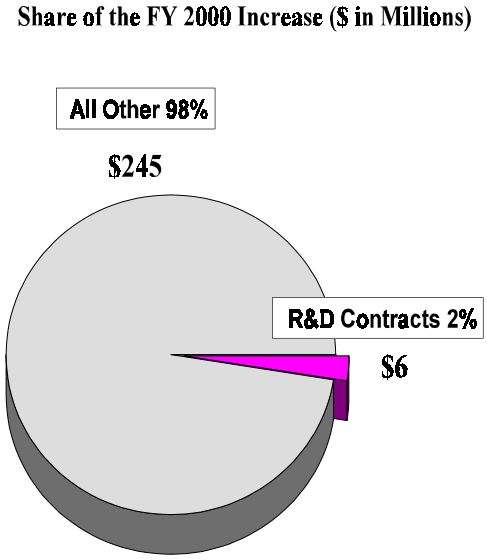
24 trainees may be supported by each institution per year. Funds may be used for stipends, training-related expenses, travel, and housing.

Minority Institutional Research Training Program (T32M) - renewal of RFA to offer T32M research training grants to minority schools and institutions to encourage enhancement of research skills by future researchers in areas of interest to the NHLBI. The programs are expected to attract students in their developmental stages; increase their awareness of medical conditions, issues, and procedures related to the heart, lung, and blood, and to sleep, and to transfusion medicine; and acquaint them with career opportunities in research in these fields. The program director at the minority school will be responsible for selection and appointment of trainees and for the overall direction of the training program. Trainees at the post-baccalaureate/pre-doctoral level must be in a relevant biomedical or behavioral science program and have a strong commitment to completing a doctoral degree. Trainees enrolled in a minority health professional school or with a doctoral degree or equivalent in a biomedical or behavioral science are also eligible. The minority institution must identify and collaborate with a research center (medical school or comparable institution) that has strong, relevant, well-established research and research training programs. The research center provides each trainee with a mentor who is recognized as an accomplished investigator in the relevant research and who will assist the advisor at the minority institution with the trainee's development and research plan. Trainees may be appointed for periods up to five years.

Trans-NIH

Institutional National Research Service Award in Sleep Research - renewal of PA to establish institutional multidisciplinary research training programs in sleep biology, sleep disorders medicine, and related research areas in order to ensure that highly trained scientists are available to address important gaps in our biomedical and biological understanding of sleep, including those outlined in the *NIH Director's Sleep Disorders Research Plan*. Sleep researchers are needed to investigate the basic biology of sleep; to explore epidemiological, behavioral, and clinical aspects of sleep-related disorders; and to develop new approaches to treat and prevent these conditions. Innovative, multidisciplinary, and collaborative training programs, with interactive training provided by investigators from different disciplines and with complementary skills, are strongly encouraged.

RESEARCH & DEVELOPMENT CONTRACTS



Definition - The NHLBI awards research and development (R&D) contracts to non-profit and commercial organizations for scientific inquiry directed towards particular areas of research and development. Their purpose is to use advances in knowledge and technology to search for solutions to specific questions. Contract performance is closely monitored by the NHLBI to help ensure accomplishment of project goals.

R&D Contracts Budget Distribution - FY 2000
2% of the increase
9% of total budget
194 contracts
$192m = total R&D Contracts

- **R&D Contracts Budget Increase Breakout**
  - $ 6m - To fund an additional 11 contracts
  - $ 6m - of the $251m increase

New and Expanded FY 2000 R&D Contract Programs

Heart and Vascular Diseases Program

Atherosclerosis Risk in Communities (ARIC) Study - Morbidity/Mortality Follow-Up - renewal of Request for Proposals (RFP) to extend for an additional seven years the NHLBI Atherosclerotic Risk in Communities (ARIC) study. ARIC, a 12-year study begun in 1987, was designed to measure the incidence of coronary heart disease (CHD) in four diverse U.S. communities and to identify factors associated with atherosclerosis and new CHD events in middle age. The community surveillance component included 315,000 residents aged 35 to 74. The cohort component included a sample of 15,792 men and women aged 45 to 64 who received four triennial clinical examinations. Findings have been presented in more than 200 publications. The extension will permit detection of incidence trends in race-sex subgroups and analyses of stored blood, urine, and DNA samples. Follow-up for cardiovascular

morbidity and mortality will identify factors related to CHD and congestive heart failure and clarify the relationship of atherosclerosis progression or regression to subsequent CVD incidence.

Coronary Artery Risk Development in Young Adults (CARDIA) Study Extension - renewal of RFP to extend for five years an ongoing NHLBI epidemiologic study of the evolution of cardiovascular risk factors and subclinical cardiovascular disease prior to middle age. The 5,115 CARDIA participants are a biracial cohort of young men and women in four communities who were recruited starting in 1985 at age 18-30 years and subsequently followed for 10 years. Over 130 papers resulting from this study have been published or are in press. The current proposal would add in Year 15 a measure of subclinical coronary atherosclerosis, namely, detection and quantification of calcium in the coronary arteries using computed tomography. Contracts are being renewed with the four existing field centers and the coordinating center, and a new contract is being awarded for a computed tomography reading center. Approximately 3,900 participants are expected to undergo a Year 15 examination and 3,100 are expected to undergo CT exams. The objectives of the five-year renewal are to: (1) measure early atherosclerosis, using noninvasive means, in persons aged 33-45; (2) identify and quantify risk factors for the early development of atherosclerosis measured noninvasively; (3) identify and quantify gene-environment interactions that contribute to the development of cardiovascular risk factors and to early atherosclerosis; and (4) determine whether significant race or gender differences exist in the risk factors for early atherosclerosis or in the gene-environment interactions that lead to the development of atherosclerosis.

Blood Diseases and Resources Program

Pediatric Hydroxyurea Phase III Clinical Trial (BABY HUG) - new RFP to test the hypothesis that hydroxyurea therapy is effective in the prevention of chronic organ damage in pediatric patients with sickle cell anemia. This six-year, phase III, randomized, double-blind, placebo-controlled clinical trial in 200 children, recruited at ages 6 months to 24 months, will be designed to answer the following questions: (1) can the onset of hydroxyurea therapy at an early age prevent damage to the lungs, kidney and spleen; (2) will hydroxyurea therapy adversely affect the rapid growth spurt associated with puberty; and (3) will hydroxyurea therapy affect the incidence of cancer seen in pediatric sickle cell anemia patients? Outcome measures will include changes over a 2-year period in brain function, pulmonary function, renal function, growth and developmental milestones, and quality of life. The trial will involve 10 clinical centers, a medical coordinating center, a drug distribution pharmacy, a blood and chemistry laboratory, and a cytogenetics laboratory.

Trans-NIH

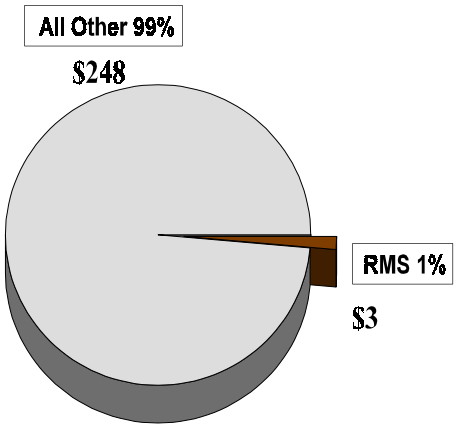
Iron Overload and Hereditary Hemochromatosis Study - new RFP to conduct an epidemiologic study on the prevalence, the genetic and environmental determinants, and the potential clinical, personal, and societal impacts of iron overload and hereditary hemochromatosis, in a multi-center, multiethnic, primary-care-based sample of 100,000 adults. This information will be used to determine the feasibility and potential individual and public health benefits and risks of primary care-based screening and intervention for iron overload and hereditary hemochromatosis. The study will consist of a Coordinating Center, five to seven Field Centers, and a Central Laboratory.

Trans-PHS

National Longitudinal Mortality Study - renewal of Inter-Agency Agreement to collect data and analyze national, secular trends in cardiovascular disease mortality in relation to a wide variety of social and economic factors. The factors include education, income, health insurance, unemployment status, retirement status, marital status, geographical location, local area economic context, ethnicity, race, family size, family composition, and occupation. The current study, initiated by the NHLBI in 1983, is composed of a population sample of 1.3 million persons from the Census Bureau Current Population Survey from 1978 to 1985 linked with mortality from the National Death Index through 1989. Phase I of this 10-year study extension would add U.S. population samples from 1986 through 1998 and would identify deaths in these samples through 1998. Phase II would consist of the routine addition of U.S. population samples and deaths yearly after 1998 through 2006. In total, the national sample will include 2 million persons and represent 200,000 deaths from 1978 to 2006.

RESEARCH MANAGEMENT AND SUPPORT (RMS)

Share of the FY 2000 Increase ($ in Millions)



Definition - The Research Management and Support (RMS) activity provides support for leadership, program guidance, planning, and evaluation for the overall management of the NHLBI programs. Major categories of support include:

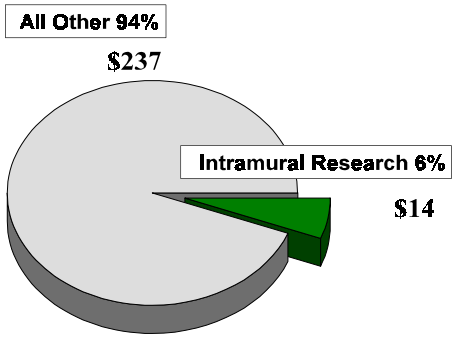
Program support for salaries and expenses for the Director, his administrative staff (financial management, personnel management, etc.), and scientific program managers. In addition to administering, managing, and reviewing research grants, research training, and R&D contract portfolios, staff are responsible for developing research initiatives in areas of scientific promise. These areas have great potential for the development of disease intervention and health promotion strategies.

RMS Budget Distribution -FY 2000
1% of the increase
3% of total budget
$66m = total RMS

- **RMS Budget Increase Breakout**
  - $ 2m - Pay FY 2000 Salary Increase (4.9%)
  - $ 1m - To support Program Oversight
  - $ 3m - of the $251m increase

INTRAMURAL RESEARCH

Share of the FY 2000 Increase ($ in Millions)



Intramural Research Budget Distribution -FY 2000
6% of the increase
6% of total budget
$119m = total Intramural Research

Definition - Through its intramural research program, the NHLBI conducts basic and clinical research at its on-campus research facilities in Bethesda, Maryland. Fundamental research performed by intramural scientists provides a basis upon which further advances in medical care are built. An important byproduct of research productivity is career development of a cadre of young physicians and basic scientists. One of the unique features of the NHLBI intramural research program is the close proximity of many of its research laboratories to the Clinical Center, a 300-350 bed research hospital on the NIH campus. This provides a unique opportunity for bridging the gap between basic and clinical science by carrying basic laboratory research to the bedside.

- **Intramural Research Budget Increase Breakout**
  - $ 5m - Pay FY 2000 Salary Increase (4.9%) and the hiring of new personnel
  - $ 4m - To increase in costs of the Minority Biomedical Training Program and all Other General Expenses
  - $ 5m - To reorganize the Division of Intramural Research, i.e., the creation of two distinct programs, the Clinical Research Program and the Laboratory Research Program.

    $ 14m - of the $251m increase